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PRE-APPEAL BRIEF REQUEST FOR REVIEW

Docket Number (Optional)
2005P56006US

I hereby certify that this correspondence is being electronically transmitted to the USPTO via EFS-Web and is addressed to: "Mail Stop AF, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450" [37 CFR 1.8(a)]

on March 27, 2008

Signature: Karen Canaan

Typed or printed name: Karen Canaan

Application Number	Filed
10/667,191	September 15, 2003

First Named Inventor: Minxue Zheng et al.

Art Unit	Examiner
1637	Heather Calamita

Applicant requests review of the final rejection in the above-identified application. No amendments are being filed with this request.

This request is being filed with a notice of appeal.

The review is requested for the reason(s) stated on the attached sheet(s).
Note: No more than five (5) pages may be provided.

I am the

- ☐ applicant/inventor.
- ☐ assignee of record of the entire interest. See 37 CFR 3.71. Statement under 37 CFR 3.73(b) is enclosed. (Form PTO/SB/96)
- ☐ attorney or agent of record. Registration number _____
- ☐ attorney or agent acting under 37 CFR 1.34. Registration number if acting under 37 CFR 1.34 42,382

Karen Canaan
Signature

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Telephone number

March 27, 2008
Date

NOTE: Signatures of all the inventors or assignees of record of the entire interest or their representative(s) are required. Submit multiple forms if more than one signature is required, see below*.

☐ *Total of 1 forms are submitted.

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In Re Application of:
John J. Quinn et al.

Confirmation No. 9085

Application Serial No. 10/667,191

Group Art Unit 1637

Filing Date: September 15, 2003

Examiner: Heather Calamita

Title: DUAL PURPOSE PRIMERS AND PROBES FOR PROVIDING ENHANCED HYBRIDIZATION ASSAYS BY DISRUPTION OF SECONDARY STRUCTURE

REMARKS IN SUPPORT OF PRE-APPEAL BRIEF REQUEST FOR REVIEW

Mail Stop AF
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

Applicants respectfully request a Pre-Appeal Brief Conference to review the legal and factual basis of the outstanding rejections for the above-referenced patent application. This paper is accompanied by a Notice of Appeal (with fee) and Form PTO/SB/33. The request for a Pre-Appeal Brief Conference is appropriate for this case because the subject application has been twice rejected and the rejections of record clearly lack the legal or factual grounds to establish a *prima facie* case of non-patentability.

THE CLAIM INTERPRETATION

The Claim Interpretation section of the Office Action was provided in response to applicants' request in the response filed on Oct. 7, 2007 (page 10, 1st full para., last sentence) for an explanation of the Office's position regarding the blocking sequence (see claim 1, item (b)). The Office's position on the blocking sequence is that it is described with functional language warranting no patentable weight. Applicants' position is that the blocking sequence is properly recited as a structural feature of the claimed dual-purpose primers. Because the Office's claim interpretation is the basis for the dispute currently before the Panel, it warrants a discussion.

In the Claim Interpretation section, it is stated that the claimed primer is described functionally because no target sequences are specified for the primer and that the claimed primer is anticipated by any prior art primer for which a target sequence exists or could be synthesized to carry out the functions of the primer. In the last full sentence at page 2, it is stated that only those limitations that impart "target-independent" structural limitations on the claimed primer will be considered. Applicants submit that the claim interpretation set forth in the Office Action is not factually or legally correct.

Although the Claim Interpretation discusses the primer generally, a review of the actual rejections in the Office Action indicates that the issue with the claimed dual-purpose primer lies only with the blocking sequence segment. Directing the Panel's attention to the anticipation rejections (*see, e.g.*, p.5,

3rd full para.), there, it is stated that the only structural limitation recited in the claims is the language directed to the primer sequence of (a). Applicants appreciate the Office's acknowledgement that the primer sequence of (a) is in fact a structural sequence; however, applicants fail to understand how the Office can consider the primer sequence of (a) to be a structural limitation, but not the blocking sequence of (b). A review of the language of (a) and (b) shows that the two claim limitations recite parallel language directed to two separate structural sequences; specifically, (a) recites a primer sequence complementary to a segment of the target nucleotide sequence other than the secondary structure forming region and (b) recites a blocking sequence substantially complementary to a segment of the secondary structure forming region. Both (a) and (b) expressly recite sequences that are part of the dual-purpose primer based upon their complementarity with sections of the target molecule.

In the responses filed on Oct. 7, 2007 (p.8 to the middle of p.10), and Jul. 27, 2007 (p.7 to the top of p.8), applicants explained how the blocking sequence is a structural feature of the claimed dual-purpose primer. The Office, however, has maintained the position that because the blocking sequence does not recite a specific sequence (i.e., a sequence reciting one or more of ATCG) (Office Action, p.3, 2nd full para.), the blocking sequence is only described with functional language. Applicants submit that the assertion that the blocking sequence is strictly a functional recitation has no factual basis. As explained in the specification, the blocking sequence prevents formation of secondary structures, which allows the dual-purpose primers to detect otherwise undetectable target nucleotides (*see*, *e.g.*, para. 0014). It is axiomatic that each target molecule will have a different sequence within the secondary structure forming region that will hybridize to the blocking sequence. In this respect, claiming the blocking sequence as requested in the Office Action would make the claimed dual-purpose primer only capable of disrupting secondary structure in a single or an extremely limited number of target molecules. Such a restriction on the claims would render any ensuing patent directed to the dual-purpose primers worthless.

Because the Claim Interpretation set forth in the Office Action is not based upon a proper factual basis, applicants respectfully request that the Panel not adopt the Claim Interpretation set forth in the Office Action; rather, applicants respectfully request that the Panel interpret the claimed dual purpose primers to include two structural limitations: the primer sequence segment of (a) and the blocking sequence segment of (b).

THE WRITTEN DESCRIPTION REJECTION

Claims 1-18 and 26-35 stand rejected under 35 U.S.C. § 112, first paragraph, as lacking an adequate written description. This rejection is respectfully traversed.

The gist of the written description rejection stems from the Claim Interpretation analysis discussed above; in short, the Office position on this issue is that because no specific sequence is specified for the target or the primer, the claim lacks an adequate written description.

In the written description rejection, citations are made to three Federal Circuit cases relating to 35 U.S.C. § 112, first paragraph. Each of the cited cases relates to new species of nucleic acids and/or proteins, all of which require a sequence or a method of isolation in order to establish possession of the compounds (*Fiers* relates to newly created human beta-interferon; *Amgen* relates to newly created human erythropoietin; and *Eli Lilly* relates to newly created human insulin protein).

In the instant case, applicants are not claiming a newly created nucleic acid or protein; rather, applicants are claiming a new general purpose primer for use in amplification experiments. Through the inclusion of a blocking sequence, the claimed dual purpose primer facilitates amplification reactions by disrupting secondary structures that otherwise prevent amplicons from being detected. The cited case law does ***not*** support the position that general purpose primers must be described with a sequence.

Because the written description rejection is not based upon a proper legal or factual basis, applicants respectfully request withdrawal of this rejection.

THE ANTICIPATION REJECTIONS

In each of the anticipation rejections of record (Wilton et al., Bannwarth et al., Laibinis et al., and Beattie et al.), the position is taken that that the only structural limitation recited in the dual purpose primer claims is the primer sequence (a). Because the Office is not giving the blocking sequence any patentable weight, the four anticipation rejections are cited for the teaching of primer sequences complementary to target nucleic acids. Applicants respectfully traverse the rejections as lacking a factual or legal basis for the reasons already of record and briefly outlined herein.

The discussion above regarding the interpretation of the claimed dual purpose primers and the arguments in traverse of the written description rejection show why the blocking sequence (b) must be given patentable weight. When the blocking sequence is given its proper patentable weight, the anticipation rejections have no factual grounds because none of the cited references teach or suggest a sequence that is comparable to the blocking sequence of the claimed dual purpose primer. The following discussion briefly summarizes the differences between the claimed invention and the cited references.

Wilton et al. teach snapback primers that are designed to produce a PCR product that *forms* secondary or tertiary structures so that the size of the PCR product may be determined by gel electrophoresis. By contrast, the blocking sequence of the claimed dual purpose primer is designed to *disrupt* secondary structure so that a site of interest within a secondary structure formation may be identified. The structural difference between the snapback primer of Wilton et al. and the dual purpose primer of the present invention is best seen when comparing Figures 1 and 3 of Wilton et al. with Figure 10 of the instant application. Wilton et al. do not teach or suggest a blocking sequence designed to disrupt secondary structure. For applicants' traversal arguments, see the responses filed on Oct. 7, 2007 (p.10, 3rd full para. to p.12); Jul. 27, 2007 (pp. 7-9); and Nov. 8, 2006 (pp. 8-9).

Bannwarth et al. teach a self-complementary oligonucleotide that backfolds upon itself in order to form a double-stranded section; the oligonucleotide formed in Bannwarth et al. is similar to the PCR product of Wilton et al. The oligonucleotide of Bannwarth et al. is shown in Figure 1. Bannwarth et al. do not teach or suggest a sequence designed to disrupt secondary structure. For applicants' traversal arguments, see the responses filed on Oct. 7, 2007 (pp. 12-13); Jul. 27, 2007 (p.9 to the top of p.10); and Nov. 8, 2006 (p.9).

Laibinis et al. teach a method for covalently linking a nucleic acid molecule having a target moiety to a support-bound oligonucleotide, i.e., a capture probe. The nucleic acid molecule is hybridized to the capture probe via a complementary sequence, i.e., a pairing sequence on the nucleic acid molecule, which is covalently bound to a complementary sequence on the capture probe. Paragraph 0010 and Figure 4 describe the oligonucleotide of Laibinis et al. Laibinis et al. do not teach or suggest a sequence designed to disrupt secondary structure. For applicants' traversal arguments, see the responses filed on Oct. 7, 2007 (pp. 13-14); Jul. 27, 2007 (p.10); and Nov. 8, 2006 (p.10).

Beattie et al. teach tandem hybridization techniques to address problems associated with nucleic acid hybridizations including the spontaneous formation of secondary structure in the single-stranded target nucleic acid. The difference between the dual purpose primers of the present invention and the tandem hybridization of Beattie et al. is most evident when Figures 5 and 10 of the instant application are compared against Figures 13A-15B of Beattie et al. Like the other references, Beattie et al. do not teach or suggest a sequence designed to disrupt secondary structure. For applicants' traversal arguments, see the responses filed on Oct. 7, 2007 (p.15 to the top of p.16) and Nov. 8, 2006 (bottom of p.10 to p.11).

Because the anticipation rejections are not based upon a proper legal or factual basis, applicants respectfully request withdrawal of this rejection.

THE OBVIOUSNESS REJECTIONS

The four obviousness rejections are directed to dependent claims. Applicants respectfully traverse the obviousness rejections for the reasons already of record. Applicants' traversal arguments for the obviousness rejections stem from the arguments presented for the anticipation rejections. For applicants' traversal arguments, see the responses filed on Oct. 7, 2007 (pp. 16-17); Jul. 27, 2007 (pp. 10-12); and Nov. 8, 2006 (pp. 11-13).

Because the obviousness rejections are not based upon a proper legal or factual basis, applicants respectfully request withdrawal of this rejection.

THE EXAMINER'S REBUTTAL ARGUMENTS

The Examiner's Rebuttal Arguments stem from the Examiner's Response to Arguments in the Office Action of Aug. 7, 2007 (pp. 14-16). There, in the sentence bridging pp. 14-15, the Examiner

acknowledges that the phrase "substantially complementary to another nucleotide sequence" from the blocking sequence recitation of the claims is a structural limitation. Nevertheless, the Examiner argued that because the term "substantially" is not defined, a single nucleotide match reads on the claims. In the response filed on Oct. 7, 2007, applicants directed the Examiner's attention to paragraph 0042 of the specification, which defines "substantially complementary" as meaning "at least about 80% complementarity." In the instant Office Action, the Examiner argues that the term "substantially complementary" is not defined because one of ordinary skill in the art would not understand the meaning of the term "at least about 80%." The Examiner's position is that the ordinary artisan would not understand the term because he or she would interpret the word "about" to include numbers on either side of 80 and the term "at least" to only include numbers less than 80 leading to indefinite confusion. Applicants position is that the word "about" is generally known to mean "approaching some degree of exactness" and that the ordinary artisan would readily understand that the word "about" in the term "at least about 80%" would only refer to those values that are slightly above 80%. Applicants arguments on this topic are found in the response filed on Oct. 7, 2007 (pp. 7-8).

Near the middle of page 17 of the Office Action, the Examiner cites *Amgen v. Chugai*, 927 F.2d 1200 (Fed. Cir. 1991) for legal support. Applicants submit that this case does not support the position taken. The *Amgen* Court did not find that the claim term "at least about 160,000" (in reference to specific activity of EPO) to be indefinite because of the language of the term; rather, the claim was held invalid because the Court found that the addition of the word "about" to the claim was an attempt to recapture mean specific activity that was anticipated by the prior art. *Amgen*, 927 F.2d at 1217-1218.

While the Examiner's position is not the subject of a rejection, because this issue concerns important claim language, applicants respectfully request that the Panel not adopt the Examiner's interpretation of the claim term "substantially complementary."

CONCLUSION

The foregoing discussion identifies the clear errors in fact and law in the rejections of record. Because the claimed invention has an adequate written description and is not anticipated or rendered obvious by the cited references, applicants respectfully request that the Panel withdraw the rejections of record and allow the subject application to pass to issue.

Respectfully submitted,

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